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09/788,793	12/16/2003	Bernard Scappi	70456	8838

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EXAMINER

HINES, JANA A

ARTICLE PAPER NUMBER

7648

DATE MAILED 07/29/2003

Please find below and or attached an Office communication concerning this application or proceeding.

Application No.

09 785,793

Applicant(s)

SERAPHIN ET AL

Office Action Summary

Examiner

Ja-Na A Hines

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

Extensions of time may be available for the payment of a fee under 37 CFR 1.136(a) to extend the period for reply, but only if the fee is paid after SIX (6) MONTHS from the mailing date of this communication.

If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.

If the period for reply specified above is the maximum statutory period, it will apply, and will expire SIX (6) MONTHS from the mailing date of this communication.

Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. 35 U.S.C. § 133.

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of
1. ☐ Certified copies of the priority documents have been received
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other _____

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DETAILED ACTION

Amendment Entry

1. The amendment entered April 8, 2003 has been entered. Claims 1 and 5 have been entered. Claims 1-11 are under consideration in this office action.

Priority

2. It is noted that applicant have failed to file a certified copy of the European application as required by 35 U.S.C. 119(b).

Withdrawal of Rejections

3. The rejection of claim 5 under 35 U.S.C. 112, second paragraph is withdrawn in view of applicants' amendments.

Response to Arguments

4. Applicant's arguments filed April 8, 2003 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. The written description rejection of claims 1-11 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in

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such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained for reasons already of record.

The rejection was based upon the written description in this case that set forth only specific polypeptides and proteins selected for detection or purification, therefore the written description is not commensurate in scope with the claims drawn to a method for detecting and or purifying substances selected from each and every protein, biomolecules, complexes of proteins or biomolecules, subunits of biomolecule complexes, cell components, cell organelles and cells.

It is noted that applicant did not respond to the written description rejection under 35 U.S.C. 112, first paragraph.

It is the examiner's position that neither the specification nor the claims provide adequate written description for a method for detecting and or purifying substances selected from each and every protein, biomolecules, complexes of proteins or biomolecules, subunits of biomolecule complexes, cell components, cell organelles and cells. There is no guidance as to what all the substances are; or what substances can or cannot be used in the method claimed. The specification does not include structural examples. It is noted that the claims no longer recite subunits thereof, however the claims generically recite a method for detecting and or purifying substances selected from each and every protein, biomolecules, complexes of proteins or biomolecules, subunits of biomolecule complexes, cell components, cell organelles and cells yet there is no adequate written description of such.

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Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

With the exception of specifically named proteins and polypeptides, the skilled artisan cannot envision the detailed structure of the substances, thus conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. An adequate description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. Furthermore, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement that defines a genus of by only their genus does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules falling within the scope of the claimed genus. Therefore only the recited proteins and polypeptides and not the full breadth of the claims meet the written description provision of 35 USC 112, first paragraph. Thus the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. The rejection of claims 1-9 and 11 under 35 U.S.C. 102(b) as being anticipated by Darzins et al., (WO 96/40943) is maintained for reasons already of record. The

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rejection was on the grounds that Darzins et al., teach a method for detecting and/or purifying substances providing an expression environment containing heterologous nucleic acids with cleavage sites encoding at the two subunits of a biomolecules, fused to at least two different affinity tags; maintaining the expression environment to allow expression of the fusion proteins with the affinity tags and detecting and or purifying the polypeptide whereby the binding of the polypeptide occurs via one affinity tag being bound to a support material.

Applicants argue that Darzins et al., do not teach the expression of proteins in native form. The instant specification defines native form to mean that a correct or relatively close to natural three-dimensional structure of the protein is achieved, i.e., the protein is folded correctly. The correct folding is of great importance because when the expressed polypeptide is a subunit of a protein it will bind to the other subunits of the complex only when it is in its native form. See page 7 lines 4-11 of the instant specification.

However, it is the examiner's position that Darzins et al., teach expressing proteins in their native form. Darzins et al., teaches that their method overcomes that problem of having formed large amounts of partially folded polypeptides gram-positive bacteria. Gram positive secretion systems provide several advantages such as being capable of exporting proteins beyond the cell wall that retain their native conformation, thereby allowing one to establish purification protocols based on the functional properties of the active protein.

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It is noted that applicants mere statements alone that Darzins et al., do not teach native form is not persuasive, since applicants have failed to provide any data supporting their accusations.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., that Darzins et al., method is not in their natural host are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants assert that Darzins et al., do not teach the use of multiple affinity tags. Applicants point to the use of sorting signals, stating that they are not affinity tags. However Darzins et al., teach the construction and use of host/vector systems that use proteins or heterologous proteins configurations fused to a combination of polyhistidine tags and protein A IgG binding domains of Staphylococcus, Factor Xa or Tobacco Etch Virus (TEV) protease cleavage sites, i.e., affinity tags.

Applicants asserts that the protease of Darzins et al., is used for a different purpose, however, it is noted that the protease of Darzins et al., achieves that same results using the same steps as those taught by the instant specification. The MPEP section 2123 teaches that patents and publications are relevant as prior art for all they contain, and the use of these references is not limited to what the inventors describe as their own inventions or to the problems with which they are concerned. They are part of the literature of the art, relevant for all they contain." *In re Heck*, 699 F.2d 1331, 1332-

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33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir.1998) Therefore applicant's argument is not persuasive.

In response to applicant's argument that the reference teaches that the desired protein is over expressed, it is noted that the claims fail to recite any limitations on protein expression with respect to over expression. Thus applicants' reliance that the instant method claims do not require over expression is not persuasive, since the claims are not limited in such a way.

Darzins et al., specifically states that several protein configurations are possible such as the presence of a combination of polyhistidine tags and protein A IgG binding domains, factor Xa or TEV protease cleavage sites. Thus Darzins et al., teach at least two affinity tags being present on the protein wherein the protein contains the cleavage site and the protein can contain an affinity tag useful in purification methods.

Applicants' assertion that Darzins et al. only describes purification of proteins from gram-positive bacteria and that the present patent application however can be applied to any organism in which recombinant DNA can be introduced. Likewise, applicants assertions about minute recovery abilities and that Darzins et al., have restricted use in its method of recovery is not persuasive because again the claims fail

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to recite any of the argued limitations. Thus applicants' reliance that the instant method claims do not require that the method be applied to any organisms; have particular recovery amounts; or have broad capabilities is not persuasive, since those limitations are not recited by the claims. Therefore these assertions are not persuasive, since the prior art method meets the limitations of the instant claims.

Thus, the rejection is maintained and applicants' arguments have not been found persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. The rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Darzins et al., (WO 96/40943) in view of Zheng et al., is maintained for reasons already of record.

The rejection was on the grounds that it would have been prima facie obvious to one having ordinary skill in the art at the time of the invention was made to exchange the affinity tags used the method for detecting and/or purifying substances providing an expression environment as taught by Darzins et al., in view of the affinity tag of Zheng et al., because Zheng et al., teach that calmodulin binding proteins can be expressed with recombinant fusion proteins, used in affinity chromatography assays and removed from fusion proteins.

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In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the use of alternative and functionally equivalent affinity tags would have been desirable to those of ordinary skill in the art based on their ability to be expressed within recombinant fusion proteins, their use in affinity chromatography assays and their ability to be removed from fusion proteins. Thus, contrary to applicant's assertion of unexpected advantages, one would have a reasonable expectation of success because one having ordinary skill in the art would have been motivated to make such a change as a mere alternative or equivalent affinity tag since Zheng et al, teach affinity chromatography and other popular tags are known in the art of affinity purification and the expected detection and purification results would have been obtained since the prior art clearly teaches the detection and purification of similar and equivalent affinity tags.

Therefore the rejection is maintained and applicant's arguments are not found persuasive.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 703-305-0487. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 703-308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ja-Na Hines
July 23, 2003

Ja-Na Hines
7/28/03